

### ***REMARKS***

Claims 1-4, 6-10, 12 and 14-26 and 28-33 are pending in the application. Claims 14-22 and 30-32 are canceled without prejudice. Claims 1 and 23 have been amended. New claims 34-37 are added. Support for the amendments to the claims can be found throughout the originally filed specification and claims. Specifically, support for the amendments to claims 1 and 23, and for new claims 34-37, can be found, for example, at page 4, lines 24-29. No new matter has been added.

Amendment of the claims should in no way be construed as an acquiescence to any of the Examiner's rejections and has been done solely to more particularly point out and distinctly claim the invention, to expedite the prosecution of the application. Applicants reserve the right to pursue the claims as originally filed in this or a separate application(s).

Applicants traverse the rejections and respectfully request reconsideration in light of the amendments and remarks.

#### ***Objection to Claim 1***

Claim 1 is objected to for being "slight awkward". The Examiner is thanked for her careful reading of the claim and proposed suggestion. In response, the Applicants have amended claim 1 as suggested by the Examiner to clarify the claim language. Accordingly, the Examiner is requested to withdraw this objection.

#### ***Rejection of Claims 1-4, 6-10, 12, 23-26, 28-29 and 33 are rejected under 35 U.S.C. 103(a)***

Claims 1-4, 6-10, 12, 23-26, 28-29 and 33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Naughton *et al* (US 2003/0007954), in view of Lu *et al.* (Circulation, 2001), Atala *et al.* (US Patent 6,479,064), MacLaughlin *et al.* (US Patent 6,692,738) and Penn *et al* (US 2004/0161412 A1, 60/405,274 and 60/424,065). Applicants traverse this rejection.

The Examiner has improperly attempted to reconstruct the patentee's claimed invention from a large number of prior art references by using the patentee's claim as a blueprint. Without

any suggestion or motivation in the prior art, it is improper to recreate the patentee's claimed invention from the prior art.

Furthermore, Applicants disagree with the statement on the bottom of Page 7 and top of Page 8 of the Office Action stating that "it would have been obvious to the skilled artisan to alternatively use injectable polymeric hydrogels, including type I collagen, or decellularized tissue, as the matrix material for culture and delivery of the cell." Applicants disagree that using an injectable polymer matrix, as recited in claim 1, is the "functional equivalent" of a three-dimensional scaffold framework. For example, contrary to the claimed method of independent claim 1, the use of the three-dimension scaffold framework is more invasive and requires, for example, surgery, implantation, and suturing.

However, in order to expedite prosecution, Applicants have amended independent claims 1 and 23, and respectfully request reconsideration in light of the claim amendments are remarks below.

As amended, independent claims 1 and 23, and claims dependent thereto, recite the step of "encapsulating the transfected cells". Support for this amendment can be found throughout the specification, and specifically, at page 4, lines 24-29. As stated in the Specification, encapsulation allows nutrients to reach the immunoprotected cells, while the VEGF proteins secreted from the cells diffuse into the surrounding tissues. Encapsulation also protects the coated cells from the immune environment. As further discussed on page 5 of the Specification, the degree of VEGF secretion and the period of delivery can be regulated by modulating the number of engineered cells which are encapsulated per microsphere, as well as the number of microspheres injected. For example, ischemic disease may require a more prolonged delivery of VEGF than a wound healing application. Dosing schedules can be manipulated using the methods of the present invention. Thus, the claimed invention describes a method of transient and local VEGF administered to promote localized angiogenesis with minimal systemic side effects.

None of the cited references teach or suggest the benefits of encapsulating the transiently transfected cells, such that the encapsulated transfected cells are protected from the immune system, while allowing the release of the growth factor (See Page 3, lines 1-4 of the Specification). Since there is no suggestion in any of the cited references that the current methods of implantation invoke harmful systemic side effects and that cell encapsulation is beneficial, there is no motivation for one skilled in the art to look for methods of cell encapsulation. Even if all of the cited prior art is combined, the salient features of the amended independent claims 1 and 23, such as *encapsulating the transfected cells*, are not disclosed.

For all the reasons recited above, it is clear that none of the cited references disclose or suggest the method of the present invention, that there is no motivation to combine these references, and that even if combined they do not disclose or suggest the method of the present invention. Thus, these references fail to disclose or suggest every element recited by independent claim 1 and 23. Because every limitation of an independent claim is imported to dependent claims, claims 2-4, 6-10, 12, 24-26, 28-29 and 33 are also allowable. These dependent claims further define the allowable subject matter recited by claims 1 and 23. Applicant, therefore, respectfully requests that the Examiner withdraw all rejections.

#### ***New Claims***

New claims 34-37 have been added. Support for new claims 34-37 can be found, for example, at page 4, lines 24-29. The new dependent claims depend from currently amended independent claims 1 or 23, which Applicants believe to be allowable in light of the above remarks.


## CONCLUSION

In summary, the above-identified patent application has been amended and reconsideration is respectfully requested for all the reasons set forth above. In the event that the amendments and remarks are not deemed to overcome the grounds for rejection, the Examiner is kindly requested to telephone the undersigned representative to discuss any remaining issues.

Respectfully submitted,

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